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# A Concept for Early Cancer Detection and Therapy

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## ABSTRACT

Early detection and treatment of breast cancer is least costly in terms of dollars, morbidity and mortality. With new early detection x-ray technology, tumors can be found, diagnosed and treated at a much smaller size than is currently possible. This paper proposes the development of a high resolution, high quality imaging system. It is a laser-driven x-ray system with time-gated detection that removes scattering noise in the image and produces resolution on the order of 10 μm. This higher resolution and higher image quality will enable the detection of one or two millimeter tumors hopefully detecting them before metastasis. We also propose that tumor detection should be followed by an immediate needle-directed, optical fiber biopsy to instantly determine if cancer is present and, if present, the tumor should immediately be given a lethal treatment of laser or x-radiation through the same needle using fiber optics or hollow waveguides. This technology will help prevent multiple interventions resulting in both the lowest overall cost and a more efficacious therapy. The approach can be stopped at the first negative (benign) indication and will help forestall repeated examination as well as reduce patient anxiety.
**Keywords:** Early detection, high-resolution x-ray, optical biopsy, waveguide-delivered therapy

## I. INTRODUCTION

Breast cancer or other cancers are less costly to treat if detected very early in their existence. Cancer begins with a single cell that doubles in number approximately every one hundred days. At this growth rate it takes seven to nine years before the tumor reaches the size of 1-2 mm where it is able to metastasize and spread through blood vessels. Unfortunately it can grow for several years more before it reaches a size easily seen by current mammography x-ray devices or by palpation. At this point the situation is far more complicated and far more expensive to treat and cure statistics are not favorable. Even if the cancer has not spread, removal is still quite invasive requiring chemotherapy and reconstructive surgery. The only way to lower costs and improve patient outcome is to detect cancer earlier. Ideally, this is at least before it is large enough to spread.

Once small tumors are detected, a method of determining the condition of the tumor is needed – i.e., are the tumors malignant or benign. We believe this test should be made immediately while the location is known very precisely and the detection apparatus can assist with location if necessary. This is the time to insert a biopsy needle as close as possible to the tumor. We also propose continued development of optical biopsy techniques in order to speed the analysis of the tumor. Some of the methods that we are working on for tissue analysis will be discussed. Conventional biopsies can also be done as a means of comparison with optical techniques until optical techniques generate strong statistically-significant results and can stand alone. If the tumor status is determined to be benign, the patient can go home without further treatment. The tumor can be watched in subsequent examinations.

If, however, the tumor is determined to be malignant, we recommend immediate therapy to kill the tumor tissue in situ while the biopsy needle is in place next to the tumor. Several techniques seem acceptable. The first technique would be to use laser energy delivered through a fiber inserted through the biopsy needle. Dr. Robinson, one of the organizers of this conference, has been an advocate of this method.. We are working on a similar technique for in situ treatment that differs only in the possible use of x-rays rather than thermal radiation. We will discuss our method and the benefits and risks of it as we see them.

We hope to convince our readers of the value, the cost savings and the reduced trauma to patients that our three pronged approach might have. We hope to spark some enthusiasm for the production of higher resolution and higher image



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quality x-ray devices that can be combined with immediate tumor analysis and immediate therapy. Optical elements and optical diagnosis and therapy also play a significant role in this plan.

## II. HIGH RESOLUTION, HIGH IMAGE QUALITY X-RAY IMAGES

Several years ago we presented the initial idea for a high-resolution, high image quality x-ray device. Much of the idea was based on a 1995 paper [1] in which Gordon et. al. used an amplified Ti:sapphire femtosecond pulse-width laser to generate hard x-rays and showed that time-gated x-ray images could remove scattered x-rays producing images with less noise and higher probability of detecting a tumor. Since the laser beam that generated the x-rays was much smaller than x-ray tube emitter sizes, a higher spatial resolution also was obtained. The combination of high resolution and higher image quality will lead to x-ray devices with the ability to find small tumors at an earlier time in their growth before they can spread to other organs.

Since smaller tumors may be more difficult to precisely locate, it is possible to split the laser beam generating the x-rays into two beams. Two beams of x-rays would allow construction of a three-dimensional image capable of providing depth information as well as x-y information thus enabling precise location of the tumors to assist accurate biopsy-needle insertion.

Generation of hard x-rays using the high power optical radiation requires more laser power than ordinary femtosecond lasers produce. High power femtosecond lasers have been generated, see Mourou, Barty and Perry [2 ], and now exist in the labs of Jeff Squier in the Colorado School of Mines and several places elsewhere. Ultrahigh power can be extracted by the process of chirped-pulse amplification of femtosecond pulse-width lasers. The basic process goes like this, First a low power femtosecond pulse is generated using a broadband gain material like Ti:sapphire. For example, say that the pulse is 20 femtoseconds in width. Putting such a short optical pulse into a gain material would damage the amplifier and distort the beam. However if the pulse is put into a pulse stretcher and stretched to a width of 20 nanoseconds, it could then be amplified without damage or distortion. After amplification to much higher energy, the pulse is compressed to its original 20 femtosecond pulsewidth. The stretcher and compressor are diffraction gratings arranged in anti-parallel and parallel configurations in a telescope of power one. These ultrahigh amplified power pulses now generate hard x-rays when focused on metal targets [3]. The type of laser system initially generated for time-gated imaging to eliminate much of the scattering noise is shown in Figure 1. Possible arrangement for generation of three-dimensional information to optimize needle insertion is shown in Figure 2.

## III. AN OPTICAL BIOPSY

A rapid biopsy is critical to our concept of rapid diagnosis and therapy. Current cancer confirmation depends on pathological inspection. It is this necessity that requires physically removing tissue and laborious laboratory procedures to process tissue and prepare thin slices for inspection under a microscope. To replace this procedure with an optically based procedure will require evaluation of the technologies available. Several potentially useful techniques are being evaluated in our laboratory. These techniques include a) a hyperspecteral technique which uses the transmission of a wide variety of wavelengths to determine the difference between normal and cancer cells; b) a confocal microscopic technique that images with fiber optics through a needle to inspect the cellular condition of the tumor detected by our high resolution x-ray; and c) a dual-confocal refractive-index, thickness measurement device that can compare the index of refraction of cancer and normal cells.

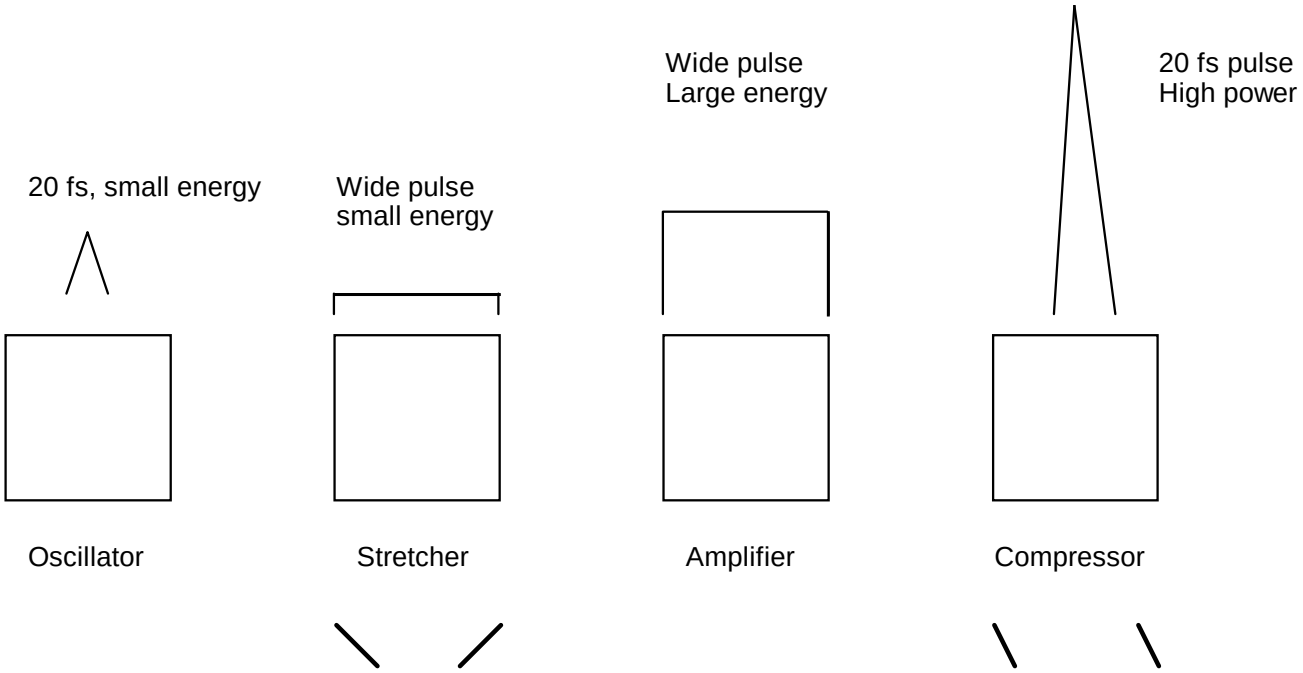


Figure 1. Diagram of Ti:sapphire chirped pulse amplification for high power laser beam to produce hard x-ray emission. [After ref # 2.]

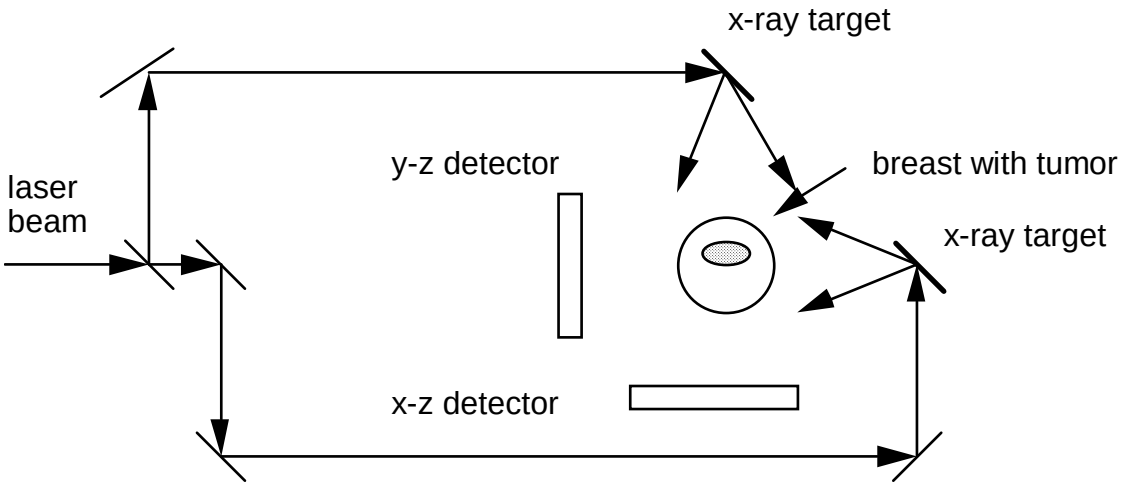


Figure 2. Arrangement of x-ray sources to enable three-dimensional location of tumor and guidance of biopsy needle.

### III.1. Hyperspectral Analysis

Much of our work has been spent in the analysis and innovative use of optical devices and sources for interrogation of tissue in all regions of the spectra from terahertz to x-ray with the conscious avoidance of the visible region of the spectrum. There has been several reasons to avoid the visible region of the spectrum. First of all there are very good fibers and sources in the visible region already. Secondly, new sources have been developed such as harmonically generated wavelengths in the UV, Vacuum Ultraviolet (VUV) and x-ray regions and Free Electron Lasers (FELs) and quantum cascade (QC) lasers in the mid-infrared (terahertz) spectral region. Thirdly, the visible region of the spectrum, as well as the near edge of the near infrared falls between the regions where electronic transitions are important and the mid-infrared regions where vibrational and rotational transitions give unique signatures that enable chemical identification. We believe interrogation of cells with mid-infrared radiation may lead to unique identification of cellular structure including the changes of this structure when cancerous conditions occur. Little work in this area has been done because material limitations increase the expense of working in these spectral regions. The recent development of the sources mentioned above requires the development of new optical techniques in order to explore these potentially fruitful spectral regions. Papers describing the optical components for mid-infrared and UV- X-ray medical devices can be found in these references [4,5]. Figure 3 shows the components useful for delivering mid-infrared to x-ray radiation.

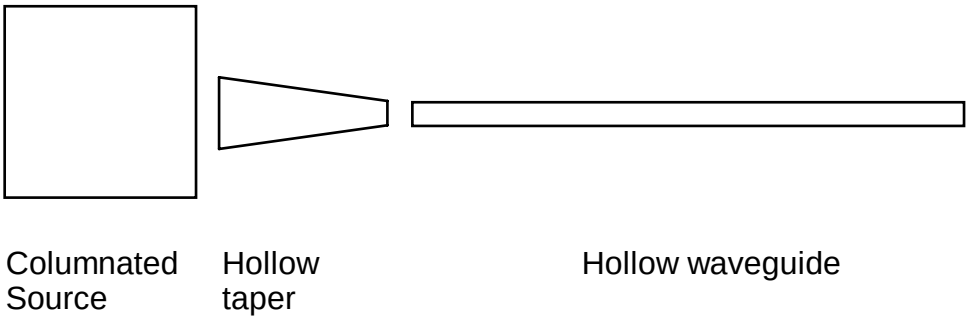


Figure 3. Delivery system for terahertz to x-ray radiation.

### III.2.Confocal Microscopic Inspection via Fiber

Confocal microscopy allows small depths of tissue to be inspected by eliminating interferences of objects above and below the depth of interest to be suppressed by a pinhole mask. A single-mode fiber of a few microns diameter can mask in the same way as is shown in a recent paper of ours [6]. The use of such a fiber as a component to bring images from tissue at the end of a fiber could enable inspection of tissue with the resolution needed for a pathological evaluation without the need to excise the tissue. This would allow rapid determination of the condition of the tumor found by high-resolution x-ray. Figure 4. Shows the use of a confocal fiber microscope for *in situ* tissue analysis.

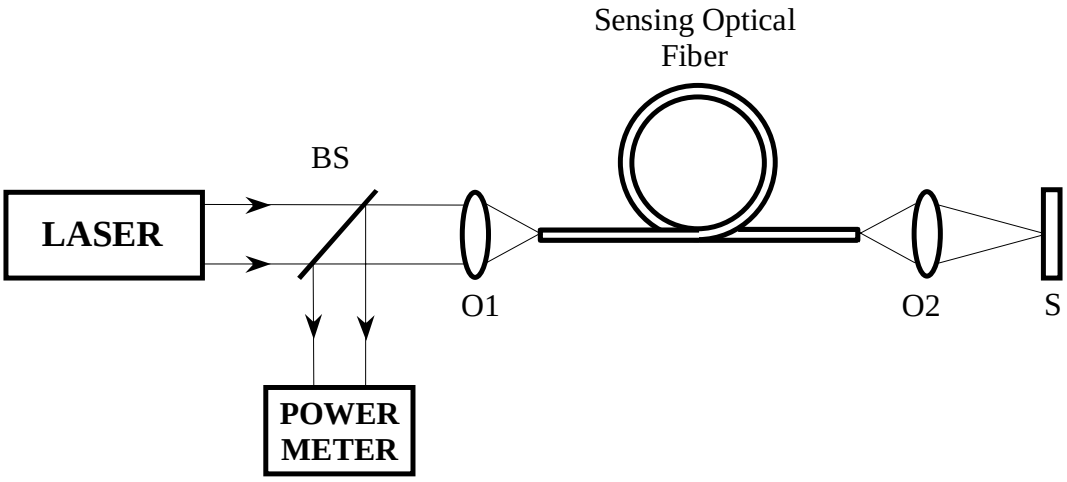


Figure 4. Fiber-Optic Confocal Microscope. Laser, He-Ne laser (632.8 nm); BS, beam-splitter cube; O1, O2, microscope objectives..

### III. 3. Dual Confocal Measurement of Refractive Index

Measurement of the index of refraction is an important optical measurement for tissue. It determines the exact path a light ray will take in tissue. All calculations depend on accurate knowledge of this fundamental parameter and we have shown a novel device that can make accurate measurements of cellular tissue

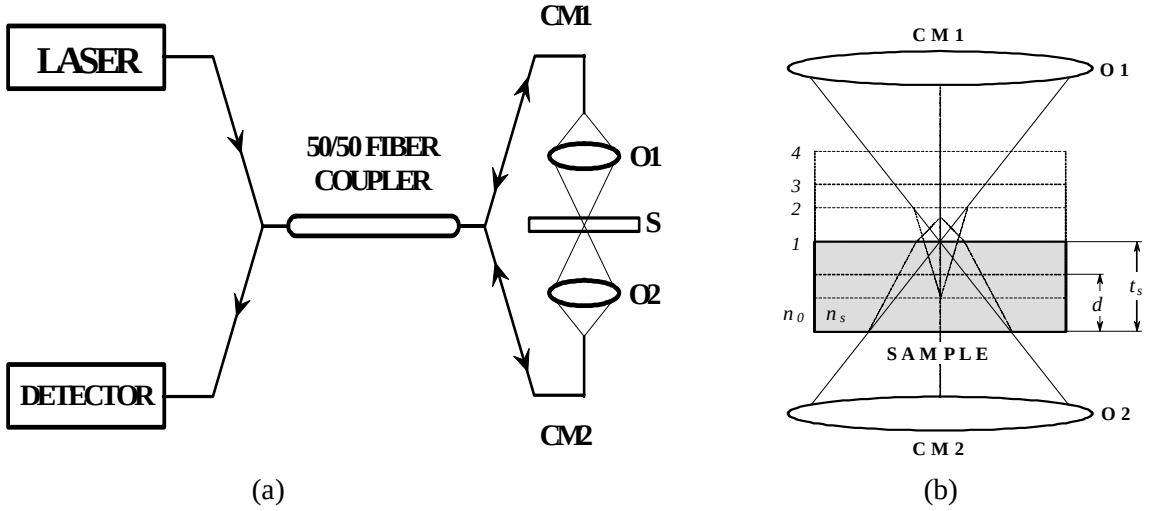


Figure 5. Experimental optical setup (a) and operating principle (b) of a dual-confocal fiber-optic sensor. Laser, He-Ne laser (632.8 nm); 50/50 Fiber Coupler, a 2×2 50/50 (3 dB) OF coupler; O1, O2, confocal focusing objectives; CM1, CM2, the first and second confocal microscope; Detector, a precise digital powermeter; $d$, sample displacement; $t_s$, sample thickness; $n_0$, refractive-index of the surrounding area; $n_s$, sample refractive-index.

components [7]. Beyond this, we are interested in the possibility that small changes in cells due to disease might be reflected in the index of refraction of cells. If so, this might also be an optical indication of the onset of cancer in some cells of a tissue. Experiments are underway to test this hypothesis. Figure 5. Shows a diagram of the embodiment of the measurement device.

Any one of these techniques for evaluating tissue could be the device needed for optical biopsy of tissue that will lead to a rapid diagnosis of cancer. Other techniques might also succeed. If any such test can accurately determine malignancy of small tumors, then the treatment of small malignant tumors by *in situ* irradiation from lasers or x-ray sources can be considered.

## IV. *IN SITU* IRRADIATION OF SMALL TUMORS

Having found small tumors and rapidly determined some to be malignant, we believe that the third step of this single mammographic visit should be the *in situ* irradiation to eradicate the tumor. We believe it is reasonable to consider *in situ* eradication of the tumor by either laser (i.e. thermal heating) or x-ray irradiation. Such treatment will require research to determine the best method of carrying out the destruction. For the laser method, consideration of the optimum heating rate and whether a single or multiple beam method will ensure killing all of the tumor with loss of minimum normal tissue will be needed. Determination of the thermal properties as well as the transmission of the tissue can help determine whether all of the tissue will reach a lethal temperature without fragmentation or ablation of the tumor. Concern should be given to the possibility of spreading the cancerous tissue without killing it should ablation take place. We have studied the delivery of x-rays by means of hollow waveguides and concentration devices and believe that the transparency of the tumor to x-rays may allow more precise treatment, but could lead to excess irradiation if good control of depth is not considered by selecting appropriate energy. Also, the possibility of amplifying x-ray killing by using oxygen gas should be considered based on observations with other irradiation [8]. Figure 6 shows the components of an x-ray delivery system for tumor irradiation..

## V. CONCLUSIONS

We believe that this concept of early tumor treatment is appropriate not only for breast cancer, but for all cancerous tumors that can be located by high-resolution imaging. We believe it is most economical to include the analysis and therapy as part of the screening process and that such procedure will cause least traumatic stress on the patient. The result of screening will be either "nothing was found" or that "a small tumor was found and taken care of during the examination." It is our hope to be able to take part in both developing the screening x-ray system and the optical diagnostic and therapeutic treatment and to see such a system used as a successful cancer therapy.

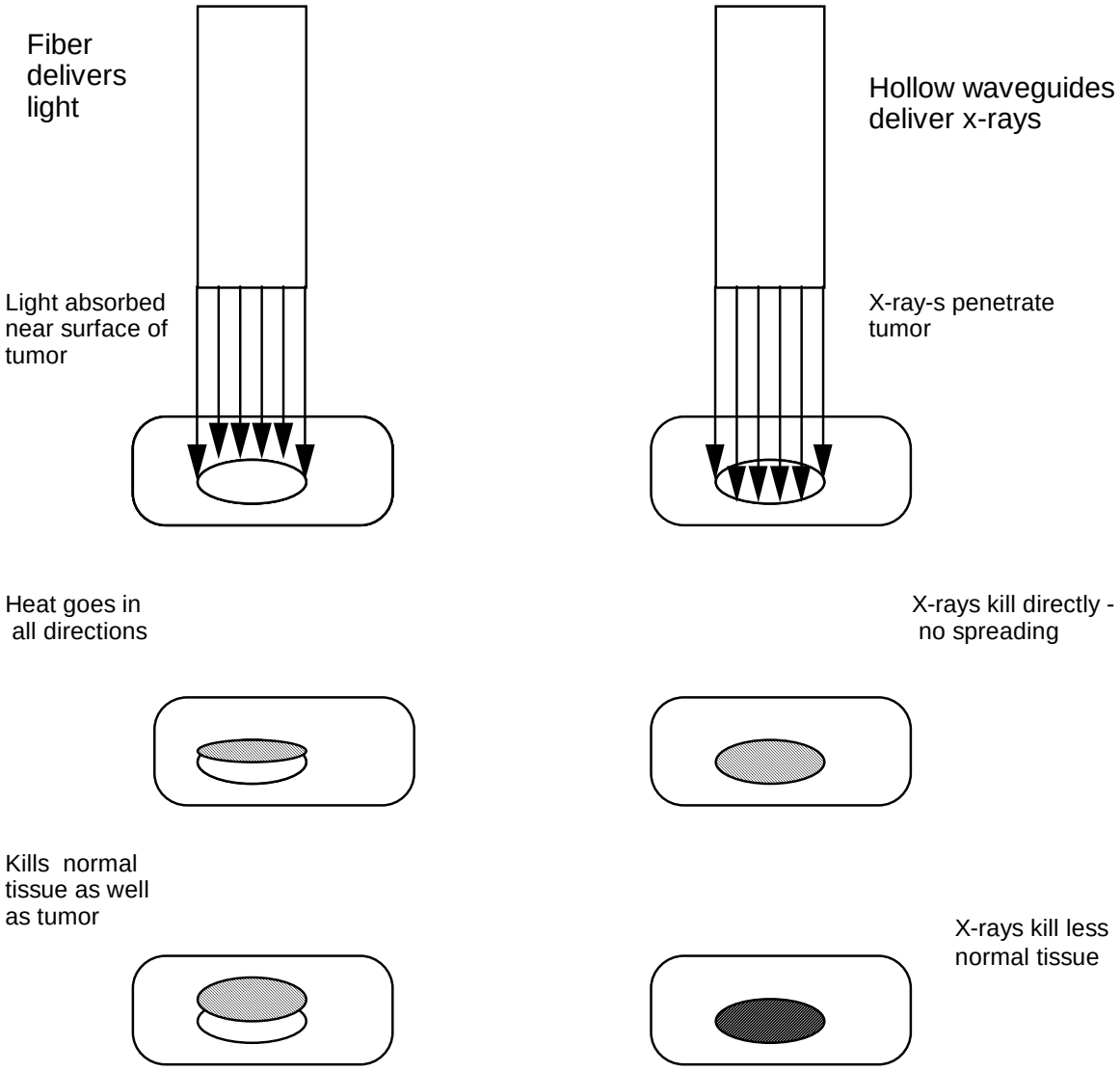


Figure 6. System used for delivery of laser radiation or x-rays for tumor irradiation.. The figure demonstrates how thermal radiation may be absorbed near the tumor surface and kill more normal tissue.

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